

Serial No.: 09/916,135
Attorney Docket No.: 3414

In the claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (currently amended) A method of reducing the complexity of a first nucleic acid sample to produce a second nucleic acid sample comprising:
 - fragmenting a first nucleic acid sample to produce fragments;
 - ligating ~~one or more adapters~~ an adaptor to the fragments to generate adaptor ligated fragments, wherein the 5' end of a first strand of an adaptor ligated fragment is complementary to the 3' end of said first strand and wherein the length of the complementary region is between 10 and 30 contiguous bases; and
 - generating said second nucleic acid sample by preferentially amplifying a plurality of the adaptor ligated fragments that are 400 to 800 base pairs in length by a polymerase chain reaction (PCR), and
 - wherein the concentration of PCR primer in said reaction is 0.4 to 0.8 μ M,
 - and said reaction comprises a plurality of cycles wherein each of said cycles comprises a step of incubation at about 72°C for between 10 and 30 seconds ~~modulating the size of the amplified fragments by varying one or more reaction conditions or reagents to reduce the complexity of the first nucleic acid sample.~~

Claims 2-15 (canceled)

16. (currently amended) The method of claim ~~15~~ 1 where the length of the PCR primer ~~said primer length~~ is 10 to 100 bases.
17. (currently amended) The method of claim ~~15~~ 1 where the length of the PCR primer ~~said primer length~~ is 15 to 50 bases.
18. (currently amended) The method of claim ~~15~~ 1 where the length of the PCR primer ~~said primer length~~ is 20 to 35 bases.

Serial No.: 09/916,135
Attorney Docket No.: 3414

19. (currently amended) The method of claim 1 where said reaction comprises ~~condition varied is the presence or absence of~~ a 3' to 5' exonuclease activity.

20. (currently amended) The method of claim 1 where said reaction comprises ~~condition varied is the inclusion of~~ one or more strand terminating nucleotides.

21. (previously presented) The method of claim 20 wherein said strand terminating nucleotides are selected from the following dideoxynucleotide triphosphates: ddATP, ddTTP, ddGTP, ddCTP and ddUTP.

22. (previously presented) The method of claim 21 wherein the ratio of dNTP to ddNTP is 100 to 1.

23. (previously presented) The method of claim 21 wherein the ratio of dNTP to ddNTP is 1000 to 1.

24. (currently amended) The method of claim 1 further comprising the step of fractionating said adaptor ligated fragments according to size by gel filtration chromatography prior to amplification.

25. (previously presented) The method of claim 1 wherein the step of fragmenting said first nucleic acid sample comprises digestion with at least one restriction enzyme.

26. (previously presented) The method of claim 1 wherein the step of fragmenting said first nucleic acid sample comprises digestion with a restriction enzyme that has a six base recognition sequence.

27. (previously presented) The method of claim 1 wherein said adaptor sequences comprise PCR primer template sequences.

Serial No.: 09/916,135
Attorney Docket No.: 3414

28. (previously presented) The method of claim 1 wherein said second nucleic acid sample comprises at least 0.01% of said first nucleic acid sample.
29. (previously presented) The method of claim 1 wherein said second nucleic acid sample comprises at least 0.5% of said first nucleic acid sample.
30. (previously presented) The method of claim 1 wherein said second nucleic acid sample comprises at least 3 % of said first nucleic acid sample.
31. (previously presented) The method of claim 1 wherein said second nucleic acid sample comprises at least 12% of said first nucleic acid sample.
32. (previously presented) The method of claim 1 wherein said second nucleic acid sample comprises at least 50% of said first nucleic acid sample.
33. (previously presented) The method of claim 1 wherein said first nucleic acid sample is genomic DNA, DNA, cDNA derived from RNA or mRNA.
- 34-49 (canceled)
50. (currently amended) A method of reducing the complexity of a first nucleic acid sample to produce a second nucleic acid sample whereby said second nucleic acid sample is obtainable by:
- fragmenting said first nucleic acid sample to produce fragments;
 - ligating adaptor sequences to both ends of said fragments to generate adaptor ligated fragments, wherein said adaptor ligated fragments comprise a region of at least 10 contiguous bases in such that the 5' end of a first strand that is perfectly complementary to a region in the 3' end of said first strand and 3' ends of the fragments are complementary to one another; and
 - generating said second nucleic acid sample by amplifying a subset of the adaptor ligated fragments, wherein adaptor ligated fragments that are between 400 and 800 base pairs are preferentially amplified, by a polymerase chain reaction (PCR)

Serial No.: 09/916,135
Attorney Docket No.: 3414

wherein said reaction comprises a single PCR primer at a concentration of 0.4 to 0.8 μ M
and wherein the incubation steps of said reaction comprise a plurality of cycles, wherein
each of said plurality of cycles comprises an extension step wherein the reaction is
incubated at about 72°C for between 10 and 30 seconds
~~a subset of fragments of a~~
~~specific size range are preferentially amplified by varying the PCR primer concentration.~~

Claims 51-56 (canceled)